

Flannery et al SID 83
w/ Berlin NT

PT New human kinases and phosphatases and polynucleotides, useful for
PT diagnosing, treating or preventing autoimmune or inflammatory disorders
PT (e.g. AIDS, allergy or anemia), multiple sclerosis, osteoarthritis,
PT cancer or hepatitis.
XX
PS Claim 5; SEQ ID No 84; 424bp; English.
XX

RESULT 9
ABX75870
ID ABX75870 standard; CDNA; 1620 BP.
XX
AC ABX75870;
XX
DT 30-APR-2003 (first entry)

Alignment of S02
w/ Berlin NT

LD 1938 JVCIA 1312
RESULT 8
AA02558
ID AA02558 standard; CDNA; 2098 BP.
XX
AC AA02558;
XX
DT 07-MAY-1999 (first entry)
XX
DE Human B1 CDNA.
XX
KW B1 protein; intracellular mediator; modulator; inflammation; cell death;
XX cell survival pathway; intracellular signalling; AIDS; cancer; human; ss:
OS Homo sapiens.
XX
PN W09855507-A2.
XX

1020

domain, CARD-3 and CARD-4 polynucleotides and proteins and a partial murine CARD-4b protein and genes. The genes and proteins of the invention are involved in the regulation of caspase activation. The caspase recruitment domain (CARD) polynucleotides, polypeptides, homologues and antibodies can be used in screening assays, detection assays, predictive medicine and therapeutic and prophylactic methods of treatment. The methods may be used to diagnose and treat patients which are suffering from a disorder associated with abnormal level or rate of apoptotic cell death, abnormal activity of the Fas/ABO-1 receptor complex, abnormal activity of the TNF receptor complex, or abnormal activity of a caspase. Diseases that may be treated include cancer (particularly follicular lymphoma, carcinomas associated with mutations in p53 and hormone-dependent tumours), autoimmune disorders (e.g. systemic lupus erythematosus, immune-mediated glomerulonephritis), viral infections, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, spinal muscular dystrophy, cerebellar degeneration, anaemia, myelodysplastic syndrome, myocardial infarction, and stroke. CARD-3 protein interacts with other cellular proteins, and so can be used for regulation of cellular proliferation and differentiation and cell survival. The CARD proteins may also be used to for screen drugs or compounds which modulate their activity. The CARD-4 gene can express a long transcript that encodes CARD-4b, a short transcript that encodes CARD-4S or two CARD-4 splice variants, CARD-4Y and CARD-4Z. This sequence encodes the human CARD-3 protein described in the method of the invention

XX

Sequence 1931 BP; 613 A; 429 C; 416 G; 473 T; 0 U; 0 Other;

SQ

Query Match 40.9%; Score 682; DB 2; Length 1931;

Best Local Similarity 99.9%; Pred. No. 0;

Matches 732; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 333 AGTTACAGAGTGTTCAGAGTCCATTACCTATGTGACAGAGAAATGGAATTATCTC 392
 DB 1151 AGTTACAGAGTGTTCAGAGTCCATTACCTATGTGACAGAGAAATGGAATTATCTC 1210
 QY 393 TGAACATTCCTTAATATGATGTCACAGAGAAATGTCATCTCAGCTCCATG 452
 DB 1211 TGAACATTCCTTAATATGATGTCACAGAGAAATGTCATCTCAGCTCCATG 1270
 QY 453 AAAATAGTGTTCCTCTGAAATTCAGAGTCCCTGCGAGCTCTCAAGACATGATTTT 512
 DB 1271 AAAATAGTGTTCCTCTGAAATTCAGAGTCCCTGCGAGCTCTCAAGACATGATTTT 1330
 QY 513 TATCTAGAAAGCTCAAGCTGTATTTTATGAGCTGATCACTGCTGGAATCACA 572
 DB 1331 TATCTAGAAAGCTCAAGCTGTATTTTATGAGCTGATCACTGCTGGAATCACA 1390
 QY 573 GTTGGGATAGACCACTTTCTGATCTCAAGGGGCTGCAATCTGTGATCAAGACCACTC 632
 DB 1391 GTTGGGATAGACCACTTTCTGATCTCAAGGGGCTGCAATCTGTGATCAAGACCACTC 1450
 QY 633 CATGCTCTTCAAGCAATATATATCACTCTCAAGCTGAGAAATCAGAACTCTGCAAGC 692
 DB 1451 CATGCTCTTCAAGCAATATATATCACTCTCAAGCTGAGAAATCAGAACTCTGCAAGC 1510
 QY 693 CTGGTATAGCCAGAGCTGATCCAGAGAAAGGGAAGACATTGTGAACCAATGACAG 752
 DB 1511 CTGGTATAGCCAGAGCTGATCCAGAGAAAGGGAAGACATTGTGAACCAATGACAG 1570
 QY 753 AAGCCCTGCTTAACAGAGCTGATCCAGAGAAAGGGAAGACATTGTGAACCAATGACAG 812
 DB 1571 AAGCCCTGCTTAACAGAGCTGATCCAGAGAAAGGGAAGACATTGTGAACCAATGACAG 1630
 QY 813 ACTATGAACCTTGAATGACAGAGCTCAAGAGCTCAAGAAAGTCAAGCAATTAAGTACAG 872
 DB 1631 ACTATGAACCTTGAATGACAGAGCTCAAGAGCTCAAGAAAGTCAAGCAATTAAGTACAG 1690
 QY 873 CTACTGACATCCAGAGGAAGATTTGCCAAAGTTATAGTACAAAATGAAAGATACAC 932
 DB 1691 CTACTGACATCCAGAGGAAGATTTGCCAAAGTTATAGTACAAAATGAAAGATACAC 1750
 QY 933 AACAAATGGCTCTTCAAGCTTACCCGAAATTAATCTTGTGTTTCAATCAACATTTTAA 992

DB 1751 AACAAATGGCTCTTCAAGCTTACCCGAAATTAATCTTGTGTTTCAATCAACATTTTAA 1810
 QY 993 ATTACTCTCAAAATTAAGCATGTAGTACTGTTTTCAGAGAAATGTGTTTCAATA 1052
 DB 1811 ATTACTCTCAAAATTAAGCATGTAGTACTGTTTTCAGAGAAATGTGTTTCAATA 1870
 QY 1053 AAGGATTTTATA 1065
 DB 1871 AAGGATTTTATA 1883

Alignment of AF027706
w/ Berlin NT

RESULT 3
AAZ09246
ID AAZ09246 standard; cDNA, 1931 BP.
AC AAZ09246;
XX 25-OCT-1999 (first entry)
XX Human CARD-3 cDNA.
XX CARD-3; caspase recruitment domain; CARD-4; regulation; detection;
XX caspase activation; detection; screening; therapy; diagnosis; disease;
XX apoptotic cell death; Fas/APO-1 receptor complex; TNF receptor complex;
XX cancer; follicular lymphoma; carcinoma; p53 mutation; viral infection;
XX hormone-dependent tumour; autoimmune disorder; Alzheimer's disease;
XX systemic lupus erythematosus; immune-mediated glomerulonephritis; stroke;
XX Parkinson's disease; amyotrophic lateral sclerosis; retinitis pigmentosa;
XX spinal muscular dystrophy; cerebellar degeneration; anaemia; drug;
XX myelodysplastic syndrome; myocardial infarction; cell proliferation;
XX cell differentiation; cell survival; CARD-4L; CARD-4S; CARD-4Y; CARD-4Z;
XX human; ds.
XX Homo sapiens.
XX OS
XX FH Key
XX CDS Location/Qualifiers
XX 214..1836
XX /*tag= a

FT XX XX
PN WO9940102-A1. /product= "CARD-3"
XX 12-AUG-1999.
PD 05-FEB-1999; 99WO-US002544.
XX 06-FEB-1998; 98US-00019942.
PR 17-JUN-1998; 98US-00099041.
PR 08-DEC-1998; 98US-00207359.
XX (MILL-) MILLENNIUM PHARM INC.
XX Berlin J;
PI WPI; 1999-494269/41.
DR P-PSDB; AAY31140.
XX Novel CARD-3 and CARD-4 genes and polypeptides used or treating
PT regulation of cellular proliferation and differentiation and cell
PT survival.
XX Example 2; Fig 1; 181pp; English.
PS This invention describes the isolation of novel human caspase recruitment
XX domain, CARD-3 and CARD-4 polynucleotides and proteins and a partial
XX murine CARD-4L protein and genes. The genes and proteins of the invention
XX are involved in the regulation of caspase activation. The caspase
XX recruitment domain (CARD) polynucleotides, polypeptides, homologues and
XX antibodies can be used in screening assays, detection assays, predictive
XX medicine and therapeutic and prophylactic methods of treatment. The
XX methods may be used to diagnose and treat patients which are suffering
XX from a disorder associated with abnormal level or rate of apoptotic cell
XX death, abnormal activity of the Fas/APO-1 receptor complex, abnormal
XX activity of the TNF receptor complex, or abnormal activity of a caspase.
XX Diseases that may be treated include cancer (particularly follicular
XX lymphoma, carcinomas associated with mutations in p53 and hormone-
XX dependent tumours), autoimmune disorders (e.g. systemic lupus
XX erythematosus, immune-mediated glomerulonephritis), viral infections,
XX Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis,
XX retinitis pigmentosa, spinal muscular dystrophy, cerebellar degeneration,
XX anaemia, myelodysplastic syndrome, myocardial infarction, and stroke.
XX CARD-3 protein interacts with other cellular proteins, and so can be used
XX for regulation of cellular proliferation and differentiation and cell
XX survival. The CARD proteins may also be used to for screen drugs or
XX compounds which modulate their activity. The CARD-4 gene can express a
XX long transcript that encodes CARD-4L, a short transcript that encodes
XX CARD-4S or two CARD-4 splice variants, CARD-4Y and CARD-4Z. This sequence
XX encodes the human CARD-3 protein described in the method of the invention
SQ Sequence 1931 BP; 613 A; 429 C; 416 G; 473 T; 0 U; 0 Other;
Query Match 74.5%; Score 1864; DB 4; Length 1931;
Best Local Similarity 99.7%; Pred. No. 5.3e-06;
Matches 1867; Conservative 0; Mismatches 5; Indels 0; Gaps 0;
QY 23 GTGAGCTCTGTTGGAGAGCAAGCGCTGCGCGGCGCATTCGGGGAATGCGGCCCTC 82
DB 12 GTGAGCTCTGTTGGAGAGCAAGCGCTGCGCGGCGCATTCGGGGAATGCGGCCCTC 71
QY 83 GTGAGCTCTGTTGGAGAGCAAGCGCTGCGCGGCGCATTCGGGGAATGCGGCCCTC 142
DB 72 GTGAGCTCTGTTGGAGAGCAAGCGCTGCGCGGCGCATTCGGGGAATGCGGCCCTC 131
QY 143 TGGGCGCTTGAAGCGCGAGTGGAGCCTTGGAGCGCGCGGAGGAGGAGCAGACCCGGA 202
DB 132 TGGGCGCTTGAAGCGCGAGTGGAGCCTTGGAGCGCGCGGAGGAGGAGCAGACCCGGA 191
QY 203 ACCGCGCTGAGCGCGCGGAGCAGTGAACGGGAGGCGCGCATTCGAGCGCGCGCATCAT 262
DB 192 ACCGCGCTGAGCGCGCGGAGCAGTGAACGGGAGGCGCGCATTCGAGCGCGCGCATCAT 251

QY 263 TCCCTACCAAACTGCCGACCTTGCGCTACTGAGCGCGCGCTCTGCGACTGTGTC 322
 DB 252 TCCCTACCAAACTGCCGACCTTGCGCTACTGAGCGCGCGCTCTGCGACTGTGTC 311
 QY 323 GTCCGCCGCCGACGAGACTGCGCGCTCAAGTGGCCCTGAGACCTGCAATCCACAC 382
 DB 312 GTCCGCCGCCGACGAGACTGCGCGCTCAAGTGGCCCTGAGACCTGCAATCCACAC 371
 QY 383 TCCGCTGCTCGACAGTGAAGAAAGAGTCTTAAAGAACTGAAATTTTACAAAGC 442
 DB 372 TCCGCTGCTCGACAGTGAAGAAAGAGTCTTAAAGAACTGAAATTTTACAAAGC 431
 QY 443 TAGATTAGTACATCTTCCAAATTTTGGAAATTTGCAATGAGCTGAAATTTTGGGAA 502
 DB 432 TAGATTAGTACATCTTCCAAATTTTGGGAAATTTGCAATGAGCTGAAATTTTGGGAA 491
 QY 503 AGTTACTGAATACATGCCAAATGATCAATTAATGAACTCTTCAATGAGAAATCTGAAT 562
 DB 492 AGTTACTGAATACATGCCAAATGATCAATTAATGAACTCTTCAATGAGAAATCTGAAT 551
 QY 563 TCCGTATGTTGCTTGGCCGACCTGAGATTTGCGATCTGCAATGAAATTTGCGTGTAA 622
 DB 552 TCCGTATGTTGCTTGGCCGACCTGAGATTTGCGATCTGCAATGAAATTTGCGTGTAA 611
 QY 623 TTACCTGCAATATGATGCTCTCTCTTACTTCAATGATGACTGAAAGCTCAATATCTT 682
 DB 612 TTACCTGCAATATGATGCTCTCTCTTACTTCAATGATGACTGAAAGCTCAATATCTT 671
 QY 683 ATTGCAATGAATTTTCAATGATGATGATTTTGGTTTATCAAAAGTGGCGCATGAT 742
 DB 672 ATTGCAATGAATTTTCAATGATGATGATTTTGGTTTATCAAAAGTGGCGCATGAT 731
 QY 743 GTCCCTCTCAAGTCAGAGAGTGAAGCAATCTGACCAAGAGAGGCAATTTATCTATAT 802
 DB 732 GTCCCTCTCAAGTCAGAGAGTGAAGCAATCTGACCAAGAGAGGCAATTTATCTATAT 791
 QY 803 GCCACCTGAAGAACTATGAACTGAGCAAAATCAAGGCGCATATCAAGCAATATATA 862
 DB 792 GCCACCTGAAGAACTATGAACTGAGCAAAATCAAGGCGCATATCAAGCAATATATA 851
 QY 863 TAGCTATGCAATTTACATGAGGAAAGTGTATCCAGAAACAGGCTTTGAAAGTGCAC 922
 DB 852 TAGCTATGCAATTTACATGAGGAAAGTGTATCCAGAAACAGGCTTTGAAAGTGCAC 911
 QY 923 CAATCCTTTGCAATATGATATGATGATGATGATGATGATGATGATGATGATGATG 982
 DB 912 CAATCCTTTGCAATATGATATGATGATGATGATGATGATGATGATGATGATGATG 971
 QY 983 AAGTTTGCATATGATATGATGATGATGATGATGATGATGATGATGATGATGATG 1042
 DB 972 AAGTTTGCATATGATATGATGATGATGATGATGATGATGATGATGATGATGATG 1031
 QY 1043 GGCACAAATCCAGTGAAGAGCATCTTCTTAAATGTTTAAATGAACTGAAACAGT 1102
 DB 1032 GGCACAAATCCAGTGAAGAGCATCTTCTTAAATGTTTAAATGAACTGAAACAGT 1091
 QY 1103 TTTGGAACATTTGAAGAGTAACTTTTCTTGAAGCTGTTATTCAGCTTAAAGAAACAA 1162
 DB 1092 TTTGGAACATTTGAAGAGTAACTTTTCTTGAAGCTGTTATTCAGCTTAAAGAAACAA 1151
 QY 1163 GTTACAGAGTGTTCAGAGTCCATTCACCTATGTCACAGAGAAATGAAATATATCTCT 1222
 DB 1152 GTTACAGAGTGTTCAGAGTCCATTCACCTATGTCACAGAGAAATGAAATATATCTCT 1211
 QY 1223 GAAACATACCTGTAATCAATGTCACAGAGAGATCAATGATGATGATGATGATGATG 1282
 DB 1212 GAAACATACCTGTAATCAATGTCACAGAGAGATCAATGATGATGATGATGATGATG 1271
 QY 1283 AATATAGTGTCTCTGAAACTCAAGTCCCTGCAAGCTCTCAAGACATGATTTTTT 1342
 DB 1272 AATATAGTGTCTCTGAAACTCAAGTCCCTGCAAGCTCTCAAGACATGATTTTTT 1331
 QY 1343 ATCTAGAAAAGCTCAAGACTGTATTTTATGAAAGTGCATCACTGCTCTGAAAATCAG 1402

DB 1332 ATCTAGAAAAGCTCAAGACTGTATTTTATGAAAGTGCATCACTGCTCTGAAAATCAG 1391
 QY 1403 TTGGGATAGCAATTTCTGTGTTCTCAAAAGGCGCATTTCTGATGATCAAGACCACTCC 1462
 DB 1392 TTGGGATAGCAATTTCTGTGTTCTCAAAAGGCGCATTTCTGATGATCAAGACCACTCC 1451
 QY 1463 ATGCTCTTCAAGCAATTAATTAATCCACTCTCACTGACAGAACTCAGAAAGTCTGACGCC 1522
 DB 1452 ATGCTCTTCAAGCAATTAATTAATCCACTCTCACTGACAGAACTCAGAAAGTCTGACGCC 1511
 QY 1523 TGTATAGCCGACAGATGATCCAGAGCAAAAGGAAACATTTGTAACCAATGACAGA 1582
 DB 1512 TGTATAGCCGACAGATGATCCAGAGCAAAAGGAAACATTTGTAACCAATGACAGA 1571
 QY 1583 AGCTGCTTACCAAGTGTGATGATGATGATGATGATGATGATGATGATGATGATGATG 1642
 DB 1572 AGCTGCTTACCAAGTGTGATGATGATGATGATGATGATGATGATGATGATGATGATG 1631
 QY 1643 CTATGACCTGTTATGATCAAGGCTCAAGGACCTCAAAAGTCAAGCAATTAATGACAC 1702
 DB 1632 CTATGACCTGTTATGATCAAGGCTCAAGGACCTCAAAAGTCAAGCAATTAATGACAC 1691
 QY 1703 TACTGACATCCAGAGAGAAATTTGCCAAAGTTATAGTACAAATTTGAAGATTAACA 1762
 DB 1692 TACTGACATCCAGAGAGAAATTTGCCAAAGTTATAGTACAAATTTGAAGATTAACA 1751
 QY 1763 ACAAATGGTCTTCAAGCTTACCCGAAATTAATGATGATGATGATGATGATGATGATG 1822
 DB 1752 ACAAATGGTCTTCAAGCTTACCCGAAATTAATGATGATGATGATGATGATGATGATG 1811
 QY 1823 TTACTCTCAAAATTAAGAGATGATGATGATGATGATGATGATGATGATGATGATGATG 1882
 DB 1812 TTACTCTCAAAATTAAGAGATGATGATGATGATGATGATGATGATGATGATGATGATG 1871
 QY 1883 AGGATATTTATA 1894
 DB 1872 AGGATATTTATA 1883

RESULT 4